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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): RIGL-008CIP

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

on xxx

Signature xxxx

Typed or printed name xxxx

Application Number	Filed
09/715,725	11-16-2000

First Named Inventor: LUO, YING

Art Unit	Examiner
1642	UNGAR, SUSAN NMN

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [X] attorney or agent of record. Registration number 48,920.
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

James S Keddie
Signature

James S. Keddie
Typed or printed name

650-833-7723
Telephone number

February 10, 2006
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of _____ forms are submitted.

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ARGUMENTS FOR PRE-APPEAL REVIEW Address to: Mail Stop: AF Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Attorney Docket No.	RIGL-008CIP
	Confirmation No.	6653
	First Named Inventor	LUO, YING
	Application Number	09/715,725
	Filing Date	November 16, 2000
	Group Art Unit	1642
	Examiner Name	UNGAR, SUSAN NMN
	Title: *"NOVEL IAPS ASSOCIATED CELL CYCLE PROTEINS, COMPOSITIONS AND METHODS OF USE"*	

Sir:

The review is requested for the reasons outlined below.

Summary Of The Claims And The Rejections

Pending claims 26, 27, 29, 30 and 32 involve ING2 polypeptides. The pending claims are provided as Exhibit 1 for the Examiners' convenience. SEQ ID NO:8 recited in the claims (and which is encoded by SEQ ID NO:7) is one of five isoforms of ING2 which are encoded by splice variants of the same gene. The sequences of all five isoforms of ING2 are set forth in the specification as SEQ ID NOS:2, 4, 6, 8 and 10.

Each of the outstanding rejections is *clearly erroneous* for at least the following reasons:

1. The grounds for the rejection of claims 26-27, 29-30 and 32 under §112, ¶1 for enablement[1] asserting the claimed subject matter has no use are substantially the same in substance as grounds that supported a now withdrawn rejection under §101.
2. The rejection of claims 27, 30 and 32 under §112, ¶1 for written description[2] is erroneous because there is clear explicit support for the claimed subject matter, and, as such, no new matter has been added.
3. The rejection of claim 27 under §112, ¶1 as lacking written description[3] contravenes the Office's own written description Guidelines. Further, no less that *five* examples of ING2 proteins are shown.
4. The rejection of claim 27 under §112, ¶1 for lack of enablement[4] is erroneous in view of the disclosure providing information about functional variants of SEQ ID NO:8 would be readily apparent because: a) SEQ ID NO:8 is a member of a well characterized family of

[1] Office Action mailed August 10, 2005, pages 2 - 10, item 3.
[2] Id. at pages 10-12, item 4.
[3] Id. at pages 12-17, item 5.
[4] Id. at pages 17-19, item 8 (there are not items 6 and 7).

proteins and b) the sequence alignment of Fig. 11 would readily suggest amino acids that could be changed.

To the extent a further discussion is believed necessary, the Review Panel is respectfully referred to the following.

1. **Rejection of claims 26-27, 29-30 and 32 under 35 U.S.C. § 112, ¶1 (enablement)**[5]

If our understanding of this 8-page rejection is correct, the Examiner argues that the specification does not enable one of skill in the art to use the invention because the asserted activity of the claimed ING2 polypeptides is questionable.

The grounds for this enablement rejection are substantially identical to the grounds to support the prior utility rejection under §101,[6] which was withdrawn in view of Applicants' arguments. Applicant understand that the law of enablement and the law of utility are different. However, there is no basis for the enablement rejection that differs from the utility rejection. This rejection appears to be clearly erroneous. Applicants have persuaded the Office that the claimed invention is useful. An enablement rejection based on *these same grounds* should likewise be withdrawn.

In short the Examiner asserts there is no nexus between SEQ ID NO:8 and either ING2b or ING2c (data is provided for ING2b (SEQ ID NO:4) and ING2c (SEQ ID NO:6) showing activation of p53, a well known tumor suppressor), and thus SEQ ID NO:8 has no use, e.g., for screening for bioactive agents that modulate p53 activity.[7] However, as detailed in prior responses, SEQ ID NOS: 2, 4, 6, 8 and 10, as well as p28ING5 (see, Shiseki *et al.* Cancer Research 63: 2373-2378, 2003) are splice variants encoded by the same gene, all share a 200 amino acid domain. As shown in Fig. 12 of the instant specification and in Shiseki *et al*, ING2b, ING2c and p28ING5 regulate expression from p53 binding site promoters. In view of this data and the high relatedness of the members of the ING2 family, one of skill in the art would reasonably conclude that SEQ ID NO:8 could be readily used in at least screening assays for identifying agents that modulate p53 activity.

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[5] Id. at pages 2 - 10, item 3.
[6] See Office Action mailed August 8, 2003, pages 4-12.
[7] Office Action mailed August 10, 2005, page 3, lines 10-11 and page 4, lines 21-23.

2. Rejection of claims 27, 30 and 32 under 35 U.S.C. § 112, ¶1 (written description)[8]

The Examiner argues that an ING2 protein that "increases activity of a promoter having a p53 binding site when introduced into a mammalian cell" is not described in the specification as filed.

This rejection is clearly erroneous. There is extensive and explicit support for the claimed subject matter at several places in the specification.[9]

The current claims recite subject matter that is no broader than as described in the specification as originally filed. As such, written description has been satisfied, and no new matter is added. This rejection should be withdrawn.

3. Rejection of claim 27 under 35 U.S.C. § 112, fist paragraph (written description)[10]

Claim 27, which recites a genus of polypeptides that have at least 95% sequence identity to SEQ ID NO:8, is rejected as failing to comply with the written description requirement of 35 U.S.C. § 112, fist paragraph.

According to the "Written Description Guidelines",[11] this claim should be adequately described. Thus, this rejection is clearly erroneous.

Example 14 of these Guidelines, which describes a scenario very similar to that currently under examination, provides an example of a specification that discloses a polypeptide sequence of SEQ ID NO:3 as having a certain activity.[12] The specification in this example also "contemplates but does not exemplify" variants of SEQ ID NO:3, and provides an assay for measuring the activity of the protein. The Guidelines state that the claimed subject matter is adequately described by the specification and the requirements of 35 USC §112 first paragraph have been met because "The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity."

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[8] Id. at pages 10-12, item 4.

[9] For example, support for such ING2 proteins can be found at page 7, lines 8-9: stating that "ING2 activates p53 binding site controlled promoters in the presence of absence of p53"; page 33, lines 5-6: stating that cell cycle proteins (of which ING2 is an example) "activate p53 binding site controlled promoters"; page 37, line 3: stating that assay employing an ING2 polypeptide can include measuring "activation of p53 binding site controlled promoters"; and Fig. 12, which shows data demonstrating that ING2 proteins (of which SEQ ID NO:8 is an example) increases transcriptional activation by p53 in a mammalian cell.

[10] Office Action mailed August 10, 2005, at pages 12-17, item 5.

[11] "Synopsis of Application of Written Description Guidelines", as published to the world wide website of the U.S.P.T.O. on March 1st, 2000.

[12] In this example, the claims are directed to polypeptides having a sequence that is at least 95% identical to that of SEQ ID NO: 3 and catalyze the reaction of A→B.

The fact pattern of this example is very similar to the instant fact pattern. The instant specification: a) describes the sequence of a full length polypeptides (i.e., SEQ ID NO:8), b) describes that SEQ ID NO:8 has IAP binding and p53-modulatory activity, c) provides detailed methods of how IAP binding activity and p53 modulatory activity can be assayed (see e.g., page 42, lines 16-27 and Fig. 12 of the instant specification).

It is the Applicants' understanding that the Written Description Guidelines were drafted and promulgated to provide a certain level of consistency in the examination of different patent applications. In order to provide consistency between the examination of different patent applications, the Guidelines should be followed, not ignored.

In addition, the instant specification is even better positioned than that of Example 14 since the splice variants SEQ ID NOS: 2, 4, 6 and 10 *are* exemplified, and in this regard several variants of SEQ ID NO:8 are indeed disclosed.

A total of *five* similar ING2 isoforms, ING2A, ING2B, ING2C, ING2D and ING2E (corresponding to SEQ ID NOS: 2, 4, 6, 8 and 10, respectively) are described in the instant specification. As such, the Applicant's claims are supported by *five* examples, of ING2 proteins, not one. The amino acid sequences of these proteins are shown in the sequence alignment of Fig. 11. In accordance with the PTO's own rules, the instant claims meet the written description requirement of §112,¶1.

Finally, withdrawal of this rejection would be consistent with recent decisions by the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office. The decisions are and *Ex parte Bandman* BAPI Appeal No. 2004-2319 (2004) and *Ex parte Sun* BAPI Appeal No. 2003-1993 (2003), among others.

The genus claims discussed in these decisions were supported by disclosure of a *single* representative species encompassed by the claims. Since the instant claims are supported by *five* examples, the Applicants submit that the instant claims should well satisfy criteria used by the Board for withdrawing this type of rejection.

4. Rejection of claim 27 under 35 U.S.C. § 112, fist paragraph (enablement)[13]

In this rejection the Examiner argues that one of skill in the art would not know which amino acids of SEQ ID NO:8 could be changed without changing the function of the protein, and thus he could not practice the full scope of the claims without undue experimentation.

[13] Id. at pages 17-19, item 8.

SEQ ID NO:8 is related to ING1, a highly characterized protein having a function similar to SEQ ID NO:8.[14] When provided the alignment of SEQ ID NO:8 and ING1 (Figure 11), the skilled person, who also has extensive knowledge of several publications on the structure/function relationship of ING1 proteins,[15] would note the conserved and non-conserved regions and amino acids between the various ING proteins in the alignment and readily use this knowledge to produce functional variants of SEQ ID NO:8. The skilled person would recognize a large number of amino acids in an ING2 protein having the sequence of SEQ ID NO:8 that may be substituted, and reasonably expect that these substitutions would have no significant effect on its function. The skilled person would also be aided by the "consensus" sequence for ING proteins at the bottom of Figure 11.

Further, the specification provides working examples of *five* of ING2 isoforms, ING2A, ING2B, ING2C, ING2D and ING2E (corresponding to SEQ ID NOS: 2, 4, 6, 8 and 10, respectively) are described in the instant application. ING2A, ING2B, ING2C and ING2E show 87.6% identity, 94.2% identity, 94.2% identity, and 81.8% to ING2D (corresponding to SEQ ID NO:8), respectively. Considering that ING2 isoforms having as little as 81.8% identity to each other can effectively can bind IAP and can induce p53, a skilled person would reasonably expect ING2 variants with *at least 95% identity* (i.e., significantly greater than 81.8% identify) to SEQ ID NO:8 to have an activity similar to that of SEQ ID NO:8. The maintenance of this rejection in light of these facts is thus clear error, **and** this rejection should be withdrawn.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: February 10, 2006

By: _____
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[14] ING1 in the prior art, but is not within the scope of claim 27.
[15] See, e.g., Zeremski (JBC 274:32172-32181, 1999; copy cited in a prior response), discusses several amino acids that are conserved between ING proteins (see Fig. 4B on page 32177 and abstract), and indicates that the conserved C-terminal domain is a "PHD" DNA binding domain (see page 32180, second column).

Exhibit 1

A complete listing of the current claims, including their status, is set for the below.

1-25. **(Cancelled)**

26. **(Previously presented)** A recombinant ING2 protein encoded by the contiguous polynucleotide sequence of nucleotides 120-845 of the nucleic acid set forth in SEQ ID NO:7.

27. **(Previously presented)** A recombinant ING2 protein, comprising an amino acid sequence having at least 95% sequence identity to the contiguous sequence set forth in SEQ ID NO:8, wherein said recombinant ING2 protein increases activity of a promoter having a p53 binding site when introduced into a mammalian cell.

28. **(Cancelled)**

29. **(Previously presented)** A recombinant ING2 protein, consisting essentially of the contiguous amino acid sequence set forth SEQ ID NO:8.

30. **(Previously presented)** The recombinant ING2 protein of claim 29, wherein said ING2 protein increases activity of a promoter having a p53 binding site when introduced into a mammalian cell.

31. **(Cancelled)**

32. **(Previously presented)** The isolated protein of claim 27, wherein said isolated protein has the contiguous amino acid sequence set forth in SEQ ID NO:8.

Exhibit 1